EXPLORATION MEDICAL CAPABILITY

# Decision Framework for Classifying the State of Knowledge for Pharmaceutical Stability in Spaceflight

Human Research Program
Exploration Medical Capability Element

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"Expanding the Boundaries of Space Medicine and Technology"

# Agenda

- Objective
- Background
- Approach
- Output
- Challenges & Limitations
- Lessons Learned

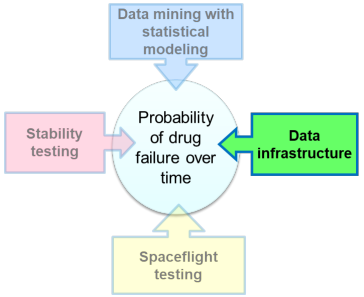
# Objective

- To develop a decision framework that will prioritize medications for future stability research based on available data.

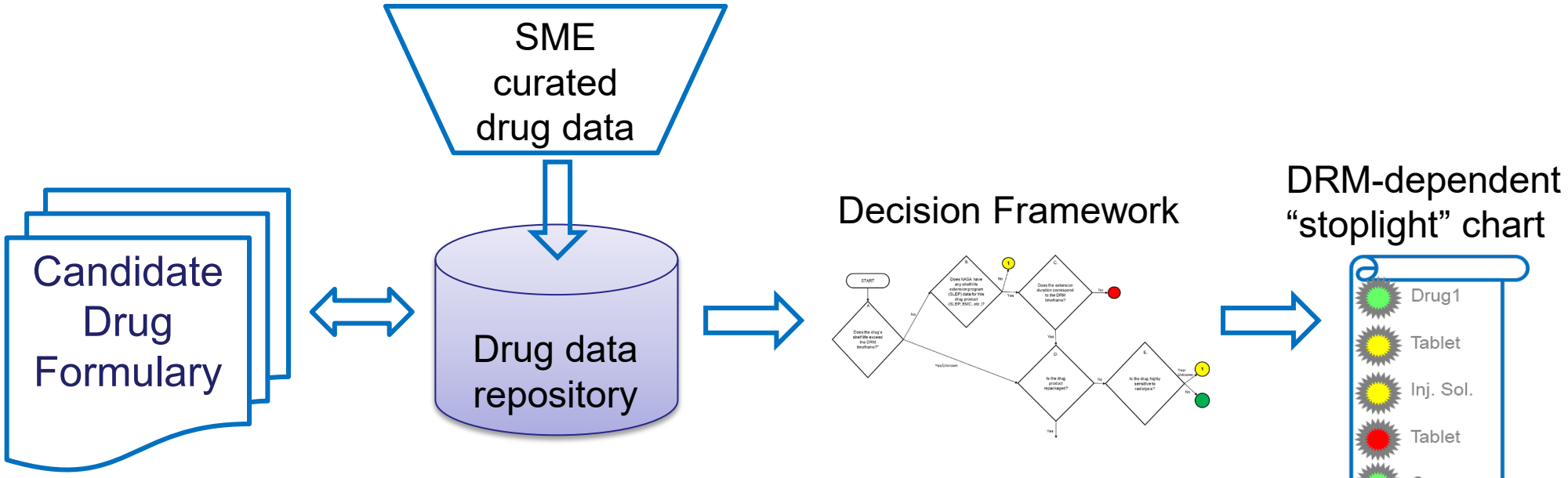
# Background

- The approved medication formulary for exploration-class spaceflight missions currently exceeds 200 pharmaceuticals. However, these medications' physical and chemical stability during long-term exposure to the spaceflight environment remains uncharacterized.
- The United States Pharmacopeia (USP) defines drug stability as "the extent to which a drug product retains, within specified limits, and throughout its period of storage and use, the same properties and characteristics that it possessed at the time of its manufacture.[1]"

# Integrated Data Infrastructure




- **Approach**




Clinical & Science Team (CST) drug resources for the treatment of medial conditions

Relational database containing drug-related data from literature, FDA and repositories

Framework for stability-risk classification of formulary drugs based on repository data

Formulary drugs classified with regards to data uncertainties for DRM

# Approach

- Team of pharmacy SMEs developed a decision framework and identified appropriate data required for drug evaluation, prioritizing:
  - Physical stability, drug quality, & safety of the active pharmaceutical ingredient (API) of finished drug products selected for specific design reference mission (DRM) drug formularies.

- Candidate medications assessed applying sequence of drug agnostic questions to evaluate limits of stability information pertinent to spaceflight.

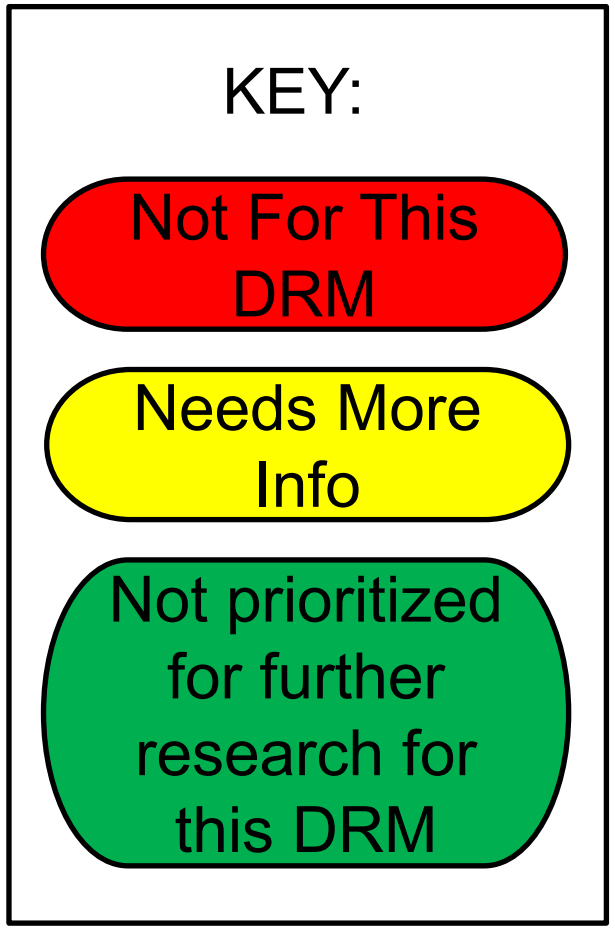
# Approach

- Decision framework relies on repository of drug information
- Includes data from multiple sources
- Informs classification of each drug product
- Resources include:
  - Authoritative, web-based databases (i.e., Drugbank, Dailymed)
  - Published literature
  - FDA/EMA drug manufacturer monographs
  - USP

# Approach

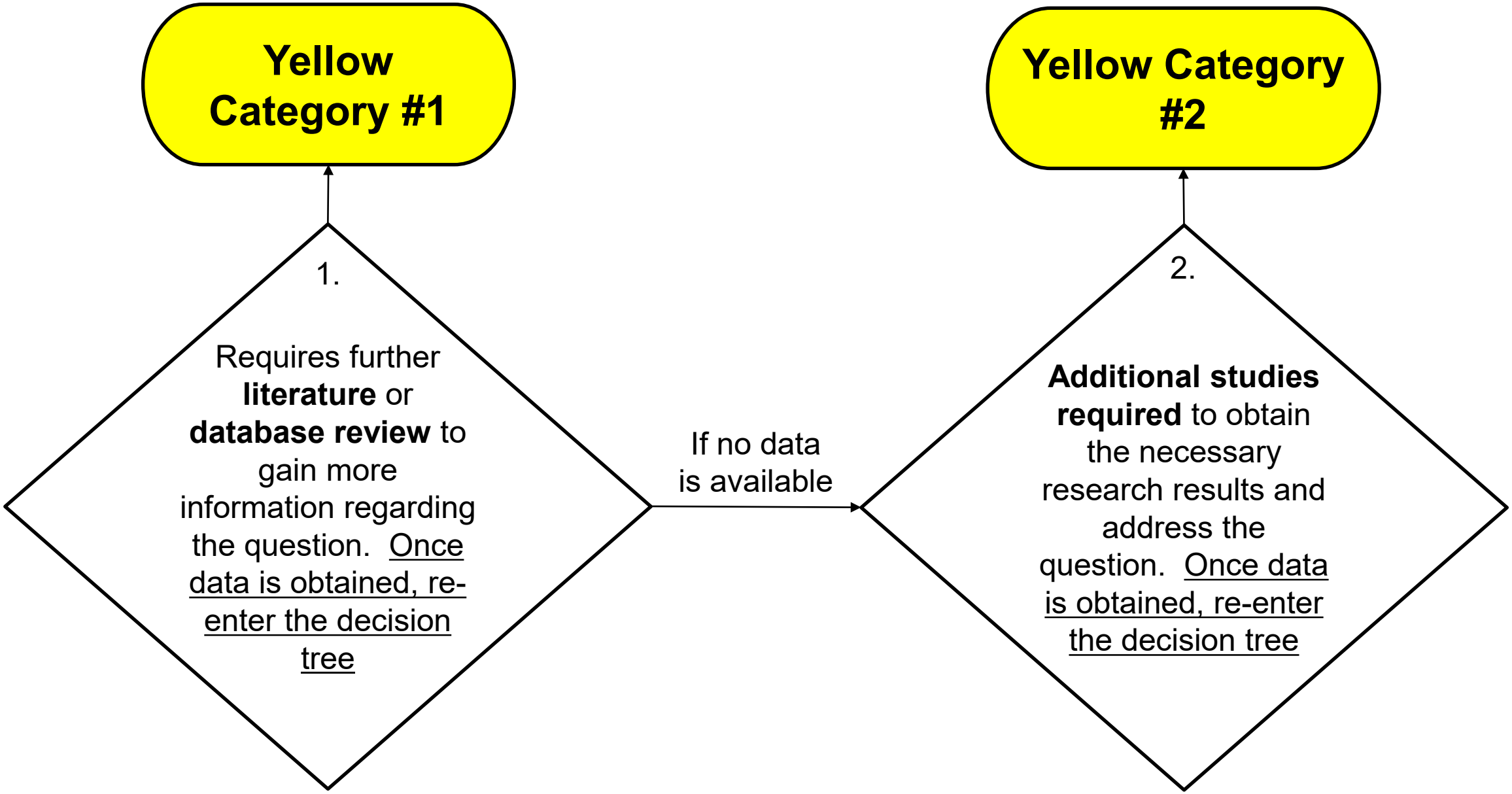
- Stoplight decision tree based on the API (not the manufactured product).
- This version of the decision tree will not be evaluating multiple manufacturers for each medication.
- Assumptions:
  - This tree is to target drugs prioritized for further evaluation/testing per DRM.
  - Environment conditions will be maintained at proper drug storage through vehicle requirements.
  - USP specifications will need to be determined for each dosage form.
  - There are no expected vacuum or vibration concerns on the vehicle.

# Approach

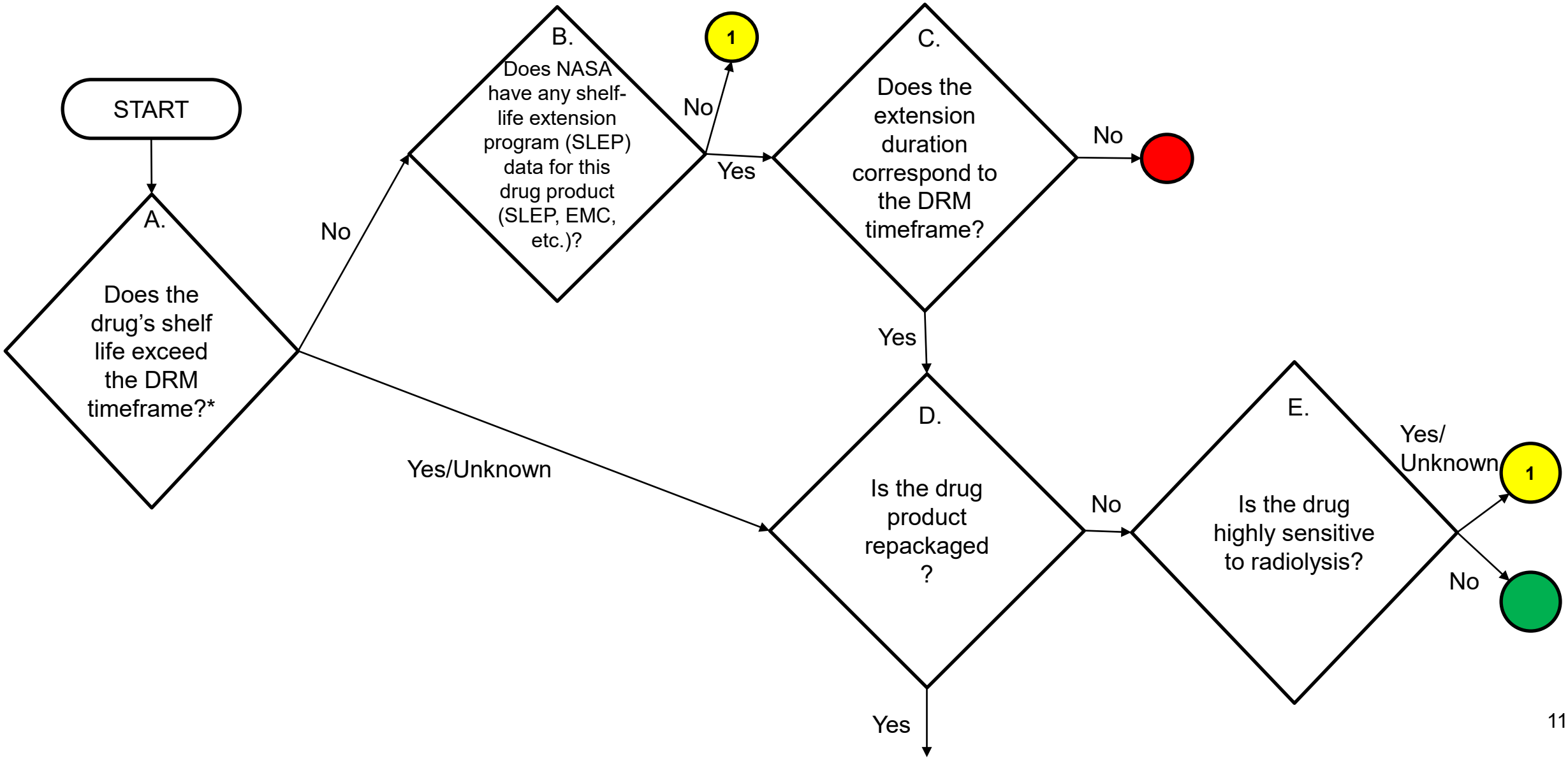



- The framework classifies each drug (API) into one of three categories:
  - Green: not prioritized for further research for this DRM
  - Yellow: requires further literature review/additional studies
  - Red: not suitable for this DRM based on current knowledge

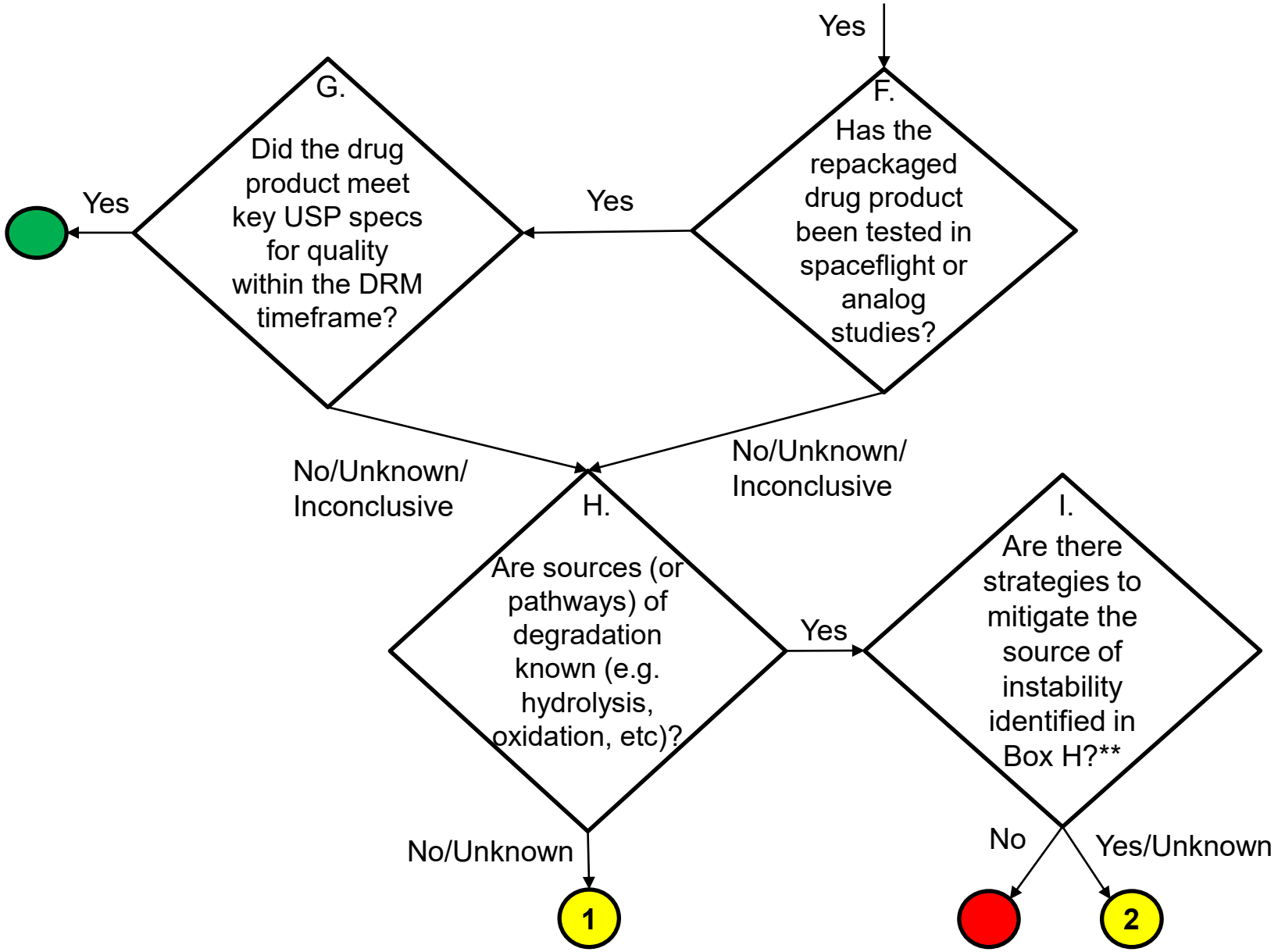
# Yellow Category



# Decision Tree



# Decision Tree (cont.)



# Output

- The results of this framework will be used to classify the state of knowledge for pharmaceutical stability for any specified DRM and guide future research efforts accordingly.

# Challenges & Limitations

- Time is lost between the start of the drug's manufacturing and the time of flight.  Real useful time in space is much less.
- Not all formulary drugs can be stability tested under spaceflight or analog conditions.
- This version will not be evaluating multiple brands/formulations for each medication.
- Before designated "green," all sources of degradation (and possibility of generating toxic degradation products) should be considered and evaluated.

# Lessons Learned

- Due to many of the medications' uncharacterized physical and chemical stability during long-term exposure to the spaceflight environment, majority of the candidate medications will fall into the yellow category – needs further testing (depending on DRM).
- Further stability testing is critical in order to appropriately characterize a drug as stable for spaceflight.

# Reference

1. *United States Pharmacopeia and National Formulary* (USP 36-NF 31). ⟨1191⟩ Stability Considerations in Dispensing Practice. Accessed March 29, 2021.

# Questions?